National Institute for Health and Care Excellence

Final

Neonatal parenteral nutrition

[J] General principles

NICE guideline NG154

Evidence reviews

February 2020

Final

These evidence reviews were developed by the National Guideline Alliance which is part of the Royal College of Obstetricians and Gynaecologists

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ISBN: 978-1-4731-3673-1

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What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Introduction

It was recognised during the stakeholder workshop and stakeholder consultation that guidance should be included on topics that could not be covered by the standard NICE guideline systematic review process. Clinical evidence reviews would not be completed on these topics due to the difficulty associated with conducting comparative clinical research where administration would be guided by physiological or pathophysiological principles or where environmental factors impact on the content of the bag (such as light protection); for examples administration of vitamins, minerals, fluid volume and electrolytes would be subject to such considerations. The body requires certain vitamins, minerals and electrolytes, and it would be unsafe and unethical to conduct studies that withheld these components. However, it was agreed that guidance on parenteral nutrition (PN) would not be complete without including general recommendations about these constituents and processes.

Due to the range of topics the committee agreed that reaching consensus by committee discussion alone would be challenging and therefore decided that a formal consensus technique should be used. They agreed that nominal group technique (the details of this are described in supplementary material C) would be an appropriate formal consensus method for producing these recommendations. These would cover overall level of included vitamins, general practice for fluid volume, overall levels of blood and urinary electrolytes, overall level of included minerals, overall level of included trace elements, delivery of lipids via syringe or bags, and filtration and protection from light.

Summary of the protocol

See Table 1 for a summary of the population, study type, publication date, publication distribution and topic areas of this review.

Table 1: Summary of the protocol

Population	• Babies born preterm, up to 28 days after their due birth date (preterm babies) • Babies born at term, up to 28 days after their birth (term babies)
Study type	• Published guidelines deemed high quality due to at least two domains scoring ≥ 70% on appraisal with the AGREE II instrument • Standard protocols, which are currently used in clinical practice
Publication date	• Published in the last 10 years • Publications prior to January 2008, excluded
Publication distribution	• International • National • Regional • Local guidelines/standard protocols, excluded
Topic areas	• Overall level of included vitamins • General practice for fluid volume • Overall levels of blood and urinary electrolytes

	• Overall level of included minerals (magnesium)* • Overall level of included trace elements • Delivery of lipids via syringe or bags • Filtration and protection from light

*The committee decided to restrict minerals to magnesium
AGREE: Appraisal of Guidelines for Research and Evaluation.

For further details see the review protocol in appendix A.

Clinical evidence

Included guidelines

Ten guidelines were identified for this review (Boullata 2014, Braegger 2018a, Braegger 2018b, Braegger 2018c, Braegger 2018d, Fusch 2009, Mihatsch 2018, Puntis 2018, van den Akker, 2018, Vanek 2018).

The included guidelines are summarised in Table 2.

See the literature search strategy in appendix B, study selection flow chart in appendix C, and study evidence tables in appendix D.

See also supplementary material C for the methods used to determine inclusion of guidelines.

Excluded guidelines

Guidelines not included in this review are listed, and reasons for their exclusions are provided in appendix K. This appendix also includes the guidelines assessed using the AGREE II tool, which were considered low quality (and therefore excluded).

Summary of clinical guidelines included in the evidence review

Summary of the guidelines that were included in this review are presented in Table 2.

Table 2: Summary of included guidelines

Study	Guideline title	Recommendations made on the topic areas of interest
Boullata 2014 US ASPEN	A.S.P.E.N. Clinical guidelines: Parenteral nutrition ordering, order review, compounding, labelling, and dispensing	• Overall level of included minerals • Delivery of lipids via syringe or bags
Braegger 2018a Europe and China ESPGHAN, ESPEN, ESPR, CSPEN	ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins	• Overall levels of included vitamins
Braegger 2018b Europe ESPGHAN, ESPEN, ESPR	ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Fluid and electrolytes	• Overall levels of blood and urinary electrolytes

Study	Guideline title	Recommendations made on the topic areas of interest
Braegger 2018c Europe ESPGHAN, ESPEN, ESPR	ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Iron and trace minerals	• Overall level of included trace elements
Braegger 2018d Europe ESPGHAN, ESPEN, ESPR	ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Complications	• General practice for fluid volume • Overall levels of blood and urinary electrolytes • Filtration and protection from light
Fusch 2009 Germany DGEM	Neonatology/Paediatrics - Guidelines on Parenteral Nutrition, Chapter 13	• Overall levels of included vitamins • General practice for fluid volume • Overall levels of blood and urinary electrolytes • Overall level of included trace elements
Mihatsch 2018 Europe and China ESPGHAN, ESPEN, ESPR, CSPEN	ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium	• Overall level of included minerals
Puntis 2018 Europe ESPGHAN, ESPEN, ESPR	ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Organisational aspects	• Delivery of lipids via syringe or bags • Filtration and protection from light
van den Akker 2018 Europe and China ESPGHAN, ESPEN, ESPR, CSPEN	ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids	• Delivery of lipids via syringe or bags • Filtration and protection from light
Vanek 2018 US ASPEN, Academy of Nutrition and Dietetics, ASHP	A call to action for optimizing the electronic health record in the parenteral nutrition workflow	• Overall levels of included vitamins • General practice for fluid volume • Overall levels of blood and urinary electrolytes • Overall level of included trace elements

ASPEN: American Society for Parenteral and Enteral Nutrition; ASHP: American Society of Health-System Pharmacists; CSPEN: Chinese Society of Parenteral and Enteral Nutrition; DGEM: German Society for Nutritional Medicine; ESPGHAN: European Society of Paediatric Gastroenterology, Hepatology and Nutrition; ESPEN: European Society for Clinical Nutrition and Metabolism; ESPR: European Society of Paediatric Research

Quality assessment of clinical guidelines included in the evidence review

Eighteen potentially relevant guidelines were assessed for quality using the AGREE II tool. Ten of these which were rated with a score of 70% or greater in 2 or more domains of the AGREE II tool were included (see appendix F for details).

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question. A single economic search was undertaken for all topics included in the scope of this guideline. Please see supplementary material D for details.

Excluded studies

No studies were identified which were applicable to this review question.

Summary of studies included in the economic evidence review

No economic evaluations were identified which were applicable to this review question.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Statements presented to the committee to rate (drafted from the included guidelines) in round 1

Twenty-eight statements were drafted using the 10 included guidelines. The draft statements covered all of the specified topic areas; overall level of included vitamins (n=7), general practice for fluid volume (n=2), overall levels of blood and urinary electrolytes (n=4), overall level of included minerals (n=4), overall level of included trace elements (n=7), delivery of lipids via syringe or bags (n=1), and filtration and protection from light (n=3). Drafted statements were presented to the committee and used in the formal consensus process.

The committee were presented with 28 statements in round 1 of the formal consensus exercise. Ten of these statements reached ≥80% agreement in round 1. Nine statements had < 60% of agreement and were discarded. Six statements had between 60% and >80% and these were redrafted for round 2. A further 3 statements that had < 60% agreement demonstrated obvious and addressable issues; these statements were redrafted for assessment by the committee in round 2.

See appendix M for the questionnaire that the committee received and the details of round 1 are provided in Table 7.

Re-drafted statements presented to the committee to rate (re-drafted from round 1) in round 2

The nine re-drafted statements were assessed by the committee in round 2.

In round 2, 7 of the 9 statements reached ≥80% agreement and were included for the discussion with the committee. The remaining 2 statements did not reach sufficient agreement and were discarded.

See Table 8 in appendix M for details of the 2 rounds.

Final agreed statements

After the 2 rounds of formal consensus the committee had reached agreement on the following 17 statements, which were subsequently discussed by the committee in order to develop the recommendations. For each topic, the agreed statements were discussed as the basis for the recommendations that the committee wanted to make on this topic. Even though the statements were agreed they were not necessarily worded in the way that the committee wanted in their recommendation or lacked a bit of detail that the committee thought would be important; therefore the agreed statements were modified using the committee's experience and expertise to develop the recommendations for these topics.

Overall level of included vitamins

- Give parenteral vitamins to infants receiving parenteral nutrition.
- Give parenteral vitamins daily to infants receiving parenteral nutrition.
- To improve vitamin stability, administer parenteral vitamin preparations together with the lipid emulsion or a mixture containing lipids.
- Parenteral lipid soluble vitamins should be given with the lipid emulsion whenever possible to remedy potential losses from vitamin oxidation.
- Give parenteral vitamins as multivitamin products to infants receiving parenteral nutrition.

General practice for fluid volume

- Tailor fluid intake in preterm and term neonates receiving parenteral nutrition according to nutritional requirements and clinical assessment, which can include but is not limited to the monitoring of humidity, specific conditions (congenital diaphragmatic hernia (CDH), and fluid balance.

Overall levels of blood and urinary electrolytes

- Maintain electrolyte homoeostasis while the infant is receiving parenteral nutrition.
- Give electrolyte supplementation (sodium, potassium, chlorine) to infants receiving parenteral nutrition as indicated by monitoring and clinical requirements.

Overall level of included minerals (magnesium)

- Provide magnesium to infants receiving parenteral nutrition.

Overall level of included trace elements

- Give parenteral trace elements to infants receiving parenteral nutrition.
- Give parenteral trace elements to infants receiving long-term parenteral nutrition.
- Give parenteral trace elements as multi-trace element products for infants receiving parenteral nutrition.
- Parenteral trace elements may be given to infants receiving parenteral nutrition as individual trace element products when an individual trace element or a specific set of trace elements are required.

Delivery of lipids via syringe or bags

- For parenteral solutions administered through a terminal filter, lipid emulsions (or all-in-one mixes) may be passed through a membrane pore size of 1.2-1.5micormetre, and aqueous solutions may be passed through a 0.22 micrometre filter.

Filtration and protection from light

- Protect bags and administration sets for use in infant parenteral nutrition from light.
- To prevent the generation of oxidants, parenteral solutions for premature infants should be protected against light.
- Protect intravenous lipid emulsions for infant parenteral nutrition by validated light-protected tubing.

Economic evidence statements

No economic evidence was identified which was applicable to this review question.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Even though the statements come from guidelines that aim to improve outcomes for babies receiving PN, in the formal consensus methodology used in this review there are no outcomes for babies that were considered formally by the committee; therefore the committee were not required to determine which outcomes were critical or important. However, the committee agreed that standard general principles in PN provision would improve outcomes for babies.

The quality of the evidence

The quality of guidelines was critically appraised by 2 reviewers using the AGREE II instrument. Ten clinical practice guidelines were deemed as high quality and were used to formulate draft statements for the formal consensus process.

Guidelines published by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), European Society for Clinical Nutrition and Metabolism (ESPEN) and European Society of Paediatric Research (ESPR), and those by ESPGHAN, ESPEN, ESPR and the Chinese Society of Parenteral and Enteral Nutrition (CSPEN) were assessed under one AGREE II appraisal as they were developed using the same methods.

Overall, included guidelines scored highly (≥ 70%) in the following 4 domains; scope and purpose, rigour of development, clarity of presentation, and editorial independence. Generally, the overall aim, specific health questions and target population for guidelines, and methods used to formulate and update the recommendations were specifically described. Guidelines detailed whether a systematic process had been used to gather and synthesise the evidence, used clear and concise language, structure, and format, and declared any bias or competing interests from guideline development group members.

Overall, guidelines scored poorly (<70%) in the following 2 domains; stakeholder involvement and applicability. Generally, guidelines were not developed by appropriate stakeholders, or did not demonstrate that the views of intended users were represented. It was unclear whether the likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guidelines were considered.

The committee noted that sometimes the statements were very similar because they came from different guidelines. They decided that this would not be a quality issue but that these minor differences between similar statements could contain important details which were discussed after the initial decision had been reached on which ones they agreed with overall.

Benefits and harms

Vitamins

Giving vitamins to babies receiving PN would reduce the likelihood of clinical and subclinical deficiency states. Therefore, the committee agreed that the introduction of vitamins to babies receiving PN should not be delayed and vitamins should be administered daily.

The committee noted that there is general agreement amongst healthcare practitioners that adding fat and water soluble vitamins to the lipid emulsion protects them from degradation; therefore, a sensible approach would be to administer vitamins with the lipid emulsion. From a practical standpoint, lipid-soluble vitamins usually come prepared in a lipid emulsion. Administering parenteral vitamin preparations together with the lipid emulsion eliminates the need to protect the infusion from light.

The committee explained that due to the use of a standard multivitamin product in the UK, giving individual parenteral vitamins to babies would be unusual practice. Most babies will receive the same amounts of vitamins via the standard multivitamin product. However in individual cases, an infant may require a specific vitamin or set of vitamins, or vitamins in different amounts than that provided by the standard multivitamin product. For safety reasons, using a licensed multicomponent product would be considered best practice. Most commercial multivitamin products are similar and therefore it is not valuable to specify which product to use in the delivery of parenteral vitamins.

Fluid volume

The amount of intravenous fluid a baby requires varies. It is common to gradually increase total intravenous fluid volume over the first few days to accommodate fluid balance in that time. As postnatal diuresis occurs intravenous fluid volume can increase. However, it may not be appropriate to increase the intravenous fluid volume, for example if the baby has kidney failure, heart failure, or hypoxic ischaemic encephalopathy then restriction of total intravenous fluid volume is required. The total intravenous fluid needed by a baby is based on multiple factors including clinical assessment of fluid balance, hydration, humidity, insensible losses and nutritional intake (parenteral and enteral).

Babies may not reach adequate levels of nutrition if clinicians prescribe PN focusing primarily on fluid volume while overlooking nutritional requirements. A common misconception among clinicians is that babies will experience fluid retention, and therefore in practice they will deliberately restrict fluids in the first few days. In reality, fluid retention is rarely a significant problem. Therefore, the primary focus should be on the nutritional needs of the baby, and the decision on fluid requirements should be secondary.

The total fluid requirement for preterm and term babies is a complex topic, and was outside the scope of this guideline. Nevertheless, it is an important factor in providing neonatal parenteral nutrition. In some situations, the total fluid allowance may be restricted or a significant proportion of the allowance might be required for other purposes (for example, other intravenous drug infusions). The committee recognised that this could result in difficulties in giving the required amount of parenteral nutrition. In order to minimise this risk, the committee agreed that standardised neonatal parenteral nutrition formulations (‘standardised bags') should use the smallest fluid volume possible. Concentrating parenteral nutrition in this way will facilitate the provision of nutritional requirements within the total fluid allowance.

Electrolytes

Babies have a maintenance requirement for electrolytes such as sodium and potassium. The electrolyte requirement will depend on a number of factors including maintenance

requirements, whether losses exceed delivery, fluid balance and whether abnormal electrolyte levels need to be corrected. Electrolyte supplementation should be given to babies receiving PN as indicated by monitoring and clinical requirements to avoid the possibility of negative effects, for example, hypo- or hypernatraemia and hypo- or hyperkalaemia. Maintenance electrolytes can be given in PN and, if needed, additional supplemental electrolytes can be given via a separate infusion to avoid the need to reformulate the PN. This guideline does not make recommendations about sodium and potassium requirements because they are affected by multiple factors unrelated to PN. PN prescribers should be aware that phosphate in PN also adds some sodium.

Minerals (magnesium)

Magnesium is required for many cell functions including energy transfer, storage and use, protein, carbohydrate and lipid metabolism, cell membrane function and regulation of parathyroid hormone secretion. It is involved in the development of the skeletal system, nervous system and muscle membranes. Consequently, PN for babies should include magnesium to prevent magnesium deficiency and reduce any possible negative effects of hypomagnesaemia including cardiac arrhythmias and seizures. Recommendations for calcium and phosphorous have been made elsewhere in this guideline (see recommendation 1.4.12 to 1.4.15) therefore these minerals were not discussed in this part of the guideline.

Trace elements

Parenteral trace elements should be given to babies receiving PN to reduce likelihood of clinical and subclinical deficiency. The use of a standard multi-trace element product, with some exceptions, is usual practice in the majority of UK neonatal units. Giving individual parenteral trace element products to babies may be necessary when a baby requires specific trace elements, or specific amounts of different trace elements, than that provided by the standard multi-trace element product. For example, babies with cholestasis have a theoretical risk of copper overload when using the some multi-trace element products. Giving individual parenteral trace element products as standard to babies would depend on the knowledge and expertise of the unit to provide a safe alternative. Therefore the committee concluded that it was not appropriate to specify which product to use in the delivery of parenteral trace elements.

Lipids via syringe or bags

The delivery of lipids via bags would ensure the stability of vitamins and the delivery of vitamins daily. While lipid bags would usually require changing every 48 hours, syringes normally require changing every 24 hours.

Filtration and protection from light

The committee discussed photo-degradation and oxidation of PN solutions, noting that this should include consideration of both aqueous and lipid components. This can be managed by light protection of both the infusion set (tubing) and the bag. The committee discussed whether a recommendation should be made to protect only the bag from light or to protect both the bag and the tubing. It is current practice that bags are protected from light. Whereas it is simple to cover the bag, to protect the tubing from light requires a different type of infusion set. It was also noted that the bag would be exposed to light for longer (because it is exposed to light whilst it hangs up during the administration of PN for up to 48 hours) whereas it is shorter for tubing because the solution moves through it. The committee agreed that light protection of the infusion set would be best practice, and are aware of recent recommendations from the European Medicines Agency (EMA) which are supported by the Medicines and Healthcare products Regulatory Agency (MHRA) to protect both the bag and

the administration sets from light. Therefore the recommendation was made to protect both the bag and the infusion sets from light.

The formal consensus process derived a statement that the committee agreed with, that lipid emulsions (or all-in-one mixes) are generally passed through a membrane pore size of 1.2-1.5 micrometre and aqueous solutions pass through a 0.22 micrometre filter. The committee discussed that theoretically the use of terminal filters could reduce particulates, precipitates and reduce systemic inflammatory response as PN can act as an effective microbiological medium against fungi, bacteria and endotoxins depending on the size of the filter. However, making up parenteral nutrition in aseptic units and using bags instead of syringes reduces the risk of bacterial contamination. Breaking a line to change the filter when running lipid from a bag was thought to pose more of an infection risk than changing the bag and filter frequently (every 48 hours)

However, current practice varies, and the formal consensus process could not agree a consensus recommendation on the use of terminal filters. The committee agreed there are still uncertainties around the benefits and harms regarding filtration, and so no recommendation was made. It was acknowledged that adding a terminal filter to the infusion set significantly adds to the expense of PN delivery.

The committee did not think that they could make any research recommendations for these topics as it would not be considered ethical to carry out comparative research into these areas (it could put babies at risk of adverse events by restricting components such as vitamins or minerals). The committee therefore prioritised research recommendations in other areas of the guideline.

Cost effectiveness and resource use

No economic studies were identified which were applicable to this review question.

The recommendations relate to the principles of care and factors that directly impact on the treatment outcomes for babies on PN. The committee expressed the view that some recommendations may have modest resource implications, which are justifiable as these principles and factors are deemed essential in ensuring the success of treatment.

Specifically, the committee discussed the high costs associated with filtration when administering PN i.e. adding a terminal filter to the infusion set makes giving parenteral nutrition significantly more expensive. They discussed that adding filters can remove particulate matter, fungi, bacteria and endotoxins depending on the size of the filter. However, making up parenteral nutrition in aseptic units and using bags instead of syringes reduces the risk of bacterial contamination. Breaking a line to change the filter when running lipid from a bag was thought to pose more of an infection risk than changing the bag and filter frequently (every 48 hours). Given these uncertainties the committee agreed that to make a recommendation on this they would require efficacy evidence as well as knowledge of costs, without which they did not think they could make a balanced, and informed decision. Overall, given the technical nature of the issue the committee decided not to make a recommendation in this area.

The committee also discussed the recommendation pertaining to the protection of bags and tubing from light, and the associated resource implications. Protecting PN by validated light-protected tubing would potentially have financial implications due to the associated expense. Shielding bags from light would be less costly. However, the committee explained that given the relatively high costs associated with PN bags, the costs associated with light protective bags and light-protected tubing might be outweighed by the potential cost savings associated with preserving the integrity of PN.

It was further explained that protecting PN bags from light is already done in most units and protecting PN tubing from light is done in some units so the impact of this recommendation

on NHS resources will be negligible. Moreover, the committee were also aware of recent recommendations from the EMA that have been endorsed by the MHRA, to protect both the bag and administration sets from light. Given that the MHRA predates the publication of this guidance and that effectiveness data was not reviewed, the committee did not consider any increase in costs due to the change in practice as a result of this guidance.

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Appendices

Appendix A – Review protocols

Review protocol for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Table 3: Review protocol for general principles for neonatal parenteral nutrition

Field (based on PRISMA-P)	Content
Review question	This chapter will cover issues that are considered important for safety and good practice of parenteral nutrition; however, these areas are not suitable for standard clinical evidence reviews as the committee do not expect formal research to have been conducted. These areas include: • Overall level of included vitamins (lipid soluble and water soluble) • General practice for fluid volume • Overall levels of blood and urinary electrolytes (Na, K, Cl,) • Overall level of included minerals • Overall level of included trace elements (zinc, fluoride, selenium, copper, chromium, iodine, manganese, and molybdenum) • Delivery of lipids via syringe or bags • Filtration and protection from light
Type of review question	Formal consensus, using nominal group technique
Objective of the review	During the stakeholder workshop as well as in the stakeholder consultation it became clear that people thought it would be important to have guidance on topics that were not going to be covered by clinical evidence reviews. The stakeholders recognised that it would not make sense to review all vitamins, minerals, fluid volume or electrolytes because the administration of these would be guided by physiological, pathophysiological and clinical principles. It is therefore impossible to conduct comparative research on these topics that can be systematically reviewed. However, stakeholders noted that guidance on parenteral nutrition would not be complete without saying something about these constituents. To be transparent and use a robust process we will use a formal nominal group exercise with the committee to reach agreement on the administration of these.
Eligibility criteria – population/disease/condition/issue/domain	• Babies born preterm, up to 28 days after their due birth date (preterm babies) • Babies born at term, up to 28 days after their birth (term babies).

Field (based on PRISMA-P)	Content
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	High quality published guidelines on neonatal parenteral nutrition, as assessed by Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument We will also look at standard protocols, which are currently used in clinical practice Only international, national or regional guidelines/standard protocols will be included (local will be excluded) We will only include guidelines published in the last ten years (January 2008 onwards) Details about AGREE II can be found here.
Eligibility criteria – comparator(s)/control or reference (gold) standard	NA
Outcomes and prioritisation	NA
Eligibility criteria – study design	Nominal group technique (NGT) The nominal group technique (Bernstein 1992) was selected due to its appropriateness for use within the guideline development process. This method, which is the most commonly used in healthcare (Murphy 1998) is effective in quickly obtaining consensus from a range of participants and is transparent, making it possible to trace how a group came to a decision and formed recommendations. The NGA technical team will extract the relevant recommendations from each guideline, and derive a set of statements or a set of proposed nutrient volume regimens (which may not be in statement format but a tabulated view). Statements will be checked for clinical content by the NGA clinical advisor and committee chair. In round 1, the committee will be presented with a consensus questionnaire with statements to be rated. They will be asked to rate their agreement based on their personal opinion of what constitutes best practice, taking into account their expertise, rather than describing current practice. Ratings should be based on agreement with the overall focus of the statement, rather than specific wording. Agreement with the statements can be rated on a 9-point Likert scale where 1 represents strongly disagree, 5 represented neither agree nor disagree and 9 represents strongly agree. Participants will also have the option of indicating that they have insufficient knowledge in a given area to provide a rating. These ratings will then be grouped into 3 categories: 1–3 (disagree), 4–6 (neither agree nor disagree), or 7–9 (agree). Participants will also be able to provide a written comment regarding their reason for any disagreement and how the statement could be modified. The NGA technical team will provide committee members with the overall percentage agreement, distribution of responses to each statement, and additional comments. Statements with greater than or equal to 80% agreement will be used to inform drafting of recommendations (taking into account comments from the committee members). Statements where there is 60 to 80% agreement will either be used to inform recommendations if the comments from committee members are consistent, and are easy to address with minor amendments, or alternatively the statements

Field (based on PRISMA-P)	Content
	will be redrafted based on the committees' comments, discussed at a committee meeting, and re-rated following the same procedure as round 1. Following the second round of rating, statements will either be used to inform recommendations, or disregarded based on percentage agreement Statements with less than 60% agreement in round 1 will be generally disregarded unless there are obvious and addressable issues identified from the comments.
Other inclusion exclusion criteria	NA
Proposed sensitivity/sub-group analysis, or meta-regression	If data allows we will write separate statements will be drafted for the following population groups: Babies born preterm, up to 28 days after their due birth date (preterm babies) Babies born at term, up to 28 days after their birth (term babies).
Selection process – duplicate screening/selection/analysis	Each identified guideline will be assessed using the AGREE II instrument by 2 independent reviewers. All disagreements will be discussed and resolved between the 2 reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the 2 reviewers. Details about AGREE II can be found here.
Data management (software)	Statements will be generated in Excel/Word
Information sources – databases and dates	Sources to be searched: Medline, Medline in-process and Embase. (Note Cochrane Library databases not searched as they do not contain guidelines). General web search for relevant guidelines conducted as well. Limits (e.g. dates, study design): limited to guidelines only For details see appendix B.
Identify if an update	This is not an update
Author contacts	Developer: the National Guideline Alliance https://www.nice.org.uk/guidance/indevelopment/gid-ng10037
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014.
Search strategy – for one database	For details please see appendix B
Data collection process – forms/duplicate	An adapted evidence table format will be used, and published as appendix D (clinical evidence tables)
Data items – define all variables to be collected	For details please see appendix B.
Methods for assessing bias at outcome/study level	NA

Field (based on PRISMA-P)	Content
Criteria for quantitative synthesis (where suitable)	NA
Methods for analysis – combining studies and exploring (in)consistency	For details of the methods please see supplementary material C.
Meta-bias assessment – publication bias, selective reporting bias	NA
Assessment of confidence in cumulative evidence	NA
Rationale/context – Current management	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance (NGA) and chaired by Joe Fawke (Consultant Neonatologist and Honorary Senior Lecturer, University Hospitals Leicester NHS Trust), in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details of the methods please see supplementary material C.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by The Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by The Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England
PROSPERO registration number	This review is not registered with PROSPERO

AGREE: Appraisal of Guidelines for Research and Evaluation; Cl: chloride; DARE: Database of Abstracts of Reviews of Effects; FIM: Functional Independence Measure; GAS: Goal Attainment Scale; GRADE: Grading of Recommendations Assessment, Development and Evaluation; GMFCS, gross motor function classification system; HTA: Health Technology Assessment; ICF: International Classification of Functioning, Disability and Health; K: potassium; MID: minimally important difference; Na: sodium; NA: not applicable; NGA: National Guideline Alliance; NGT: nominal group technique; NHS: National health service; NICE: National Institute for Health and Care Excellence; PROSPERO: International prospective register of systematic reviews; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Literature search strategies for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Databases: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	INFANT, NEWBORN/
2	(neonat$ or newborn$ or new-born$ or baby or babies).ti,ab.
3	PREMATURE BIRTH/
4	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 (birth? or born)).ab,ti.
5	exp INFANT, PREMATURE/
6	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 infan$).ti,ab.
7	(pre#mie? or premie or premies).ti,ab.
8	exp INFANT, LOW BIRTH WEIGHT/
9	(low adj3 birth adj3 weigh$ adj5 infan$).ti,ab.
10	((LBW or VLBW) adj5 infan$).ti,ab.
11	INTENSIVE CARE, NEONATAL/
12	INTENSIVE CARE UNITS, NEONATAL/
13	NICU?.ti,ab.
14	or/1-13
15	exp CHILD/
16	child$.ti,ab.
17	exp INFANT/
18	infan$.ti,ab.
19	exp PEDIATRICS/
20	p?ediatric$.ti,ab.
21	or/15-20
22	PARENTERAL NUTRITION/
23	PARENTERAL NUTRITION, TOTAL/
24	PARENTERAL NUTRITION SOLUTIONS/
25	ADMINISTRATION, INTRAVENOUS/ and (nutrition$ or feed$ or fed$).ti,ab.
26	INFUSIONS, INTRAVENOUS/ and (nutrition$ or feed$ or fed$).ti,ab.
27	CATHETERIZATION, CENTRAL VENOUS/ and (nutrition$ or feed$ or fed$).ti,ab.
28	exp CATHETERIZATION, PERIPHERAL/ and (nutrition$ or feed$ or fed$).ti,ab.
29	((parenteral$ or intravenous$ or intra-venous$ or IV or venous$ or infusion?) adj3 (nutrition$ or feed$ or fed$)).ti,ab.
30	((peripheral$ or central$) adj3 line? adj3 (nutrition$ or feed$ or fed$)).ti,ab.
31	(catheter$ adj3 (nutrition$ or feed$ or fed$)).ti,ab.
32	(drip? adj3 (nutrition$ or feed$ or fed$)).ti,ab.
33	or/22-32
34	exp GUIDELINE/
35	guideline.pt.
36	guideline?.ti.
37	or/34-36
38	(standard$ adj3 protocol?).ti.
39	"European Society of Paediatric Gastroenterology, Hepatology and Nutrition".ti,ab.
40	ESPGHAN.ti,ab.
41	"European Society for Clinical Nutrition and Metabolism".ti,ab.
42	ESPEN.ti,ab.
43	"European Society of Paediatric Research".ti,ab.
44	ESPR.ti,ab.
45	"American Society for Parenteral and Enteral Nutrition".ti,ab.
46	ASPEN.ti,ab.
47	"British Association for Parenteral and Enteral Nutrition".ti,ab.
48	BAPEN.ti,ab.
49	"The Parenteral and Enteral Nutrition Group of the British Dietetic Association".ti,ab.
50	PENG.ti,ab.
51	"The British Society of Paediatric Gastroenterology, Hepatology and Nutrition".ti,ab.
52	BSPGHAN.ti,ab.
53	"National Nurses Nutrition Group".ti,ab.
54	NNNG.ti,ab.
55	"Patients on Intravenous and Nasogastric Nutrition Therapy".ti,ab.
56	PINNT.ti,ab.
57	"British Pharmaceutical Nutrition Group".ti,ab.
58	BPNG.ti,ab.
59	"British Association of Perinatal Medicine".ti,ab.

#	Searches
60	BAPM.ti,ab.
61	or/39-60
62	(14 or 21) and 33 and 37
63	(14 or 21) and 33 and 38
64	(14 or 21) and 33 and 61
65	or/62-64
66	limit 65 to english language

Databases: Embase; and Embase Classic

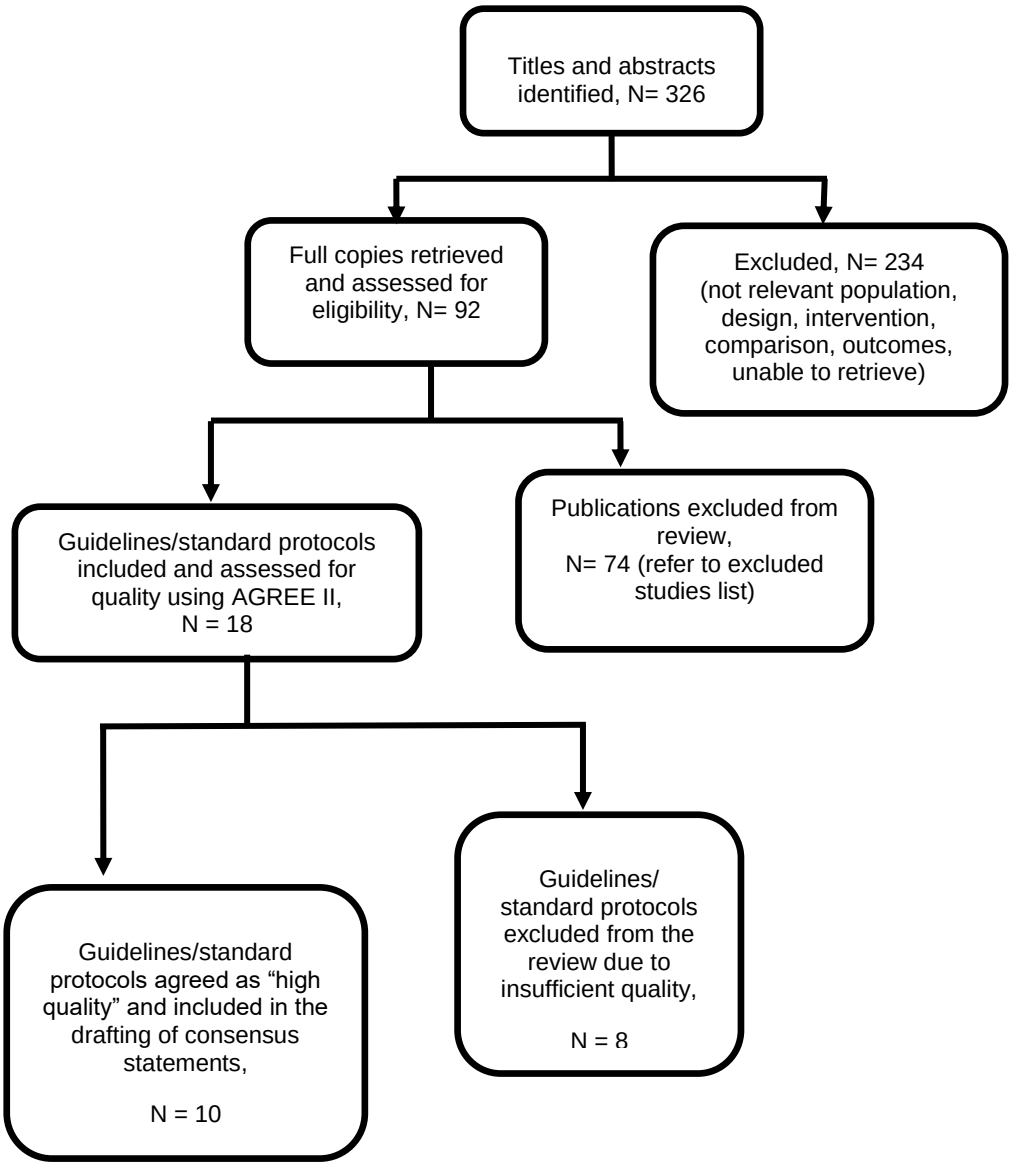
#	Searches
1	NEWBORN/
2	(neonat$ or newborn$ or new-born$ or baby or babies).ti,ab.
3	PREMATURITY/
4	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 (birth? or born)).ab,ti.
5	((preterm$ or pre-term$ or prematur$ or pre-matur$) adj5 infan$).ti,ab.
6	(pre#mie? or premie or premies).ti,ab.
7	exp LOW BIRTH WEIGHT/
8	(low adj3 birth adj3 weigh$ adj5 infan$).ti,ab.
9	((LBW or VLBW) adj5 infan$).ti,ab.
10	NEWBORN INTENSIVE CARE/
11	NEONATAL INTENSIVE CARE UNIT/
12	NICU?.ti,ab.
13	or/1-12
14	exp CHILD/
15	child$.ti,ab.
16	exp INFANT/
17	infan$.ti,ab.
18	exp PEDIATRICS/
19	p?ediatric$.ti,ab.
20	or/14-19
21	PARENTERAL NUTRITION/
22	TOTAL PARENTERAL NUTRITION/
23	PERIPHERAL PARENTERAL NUTRITION/
24	PARENTERAL SOLUTIONS/
25	INTRAVENOUS FEEDING/
26	INTRAVENOUS DRUG ADMINISTRATION/ and (nutrition$ or feed$ or fed$).ti,ab.
27	exp INTRAVENOUS CATHETER/ and (nutrition$ or feed$ or fed$).ti,ab.
28	((parenteral$ or intravenous$ or intra-venous$ or IV or venous$ or infusion?) adj3 (nutrition$ or feed$ or fed$)).ti,ab.
29	((peripheral$ or central$) adj3 line? adj3 (nutrition$ or feed$ or fed$)).ti,ab.
30	(catheter$ adj3 (nutrition$ or feed$ or fed$)).ti,ab.
31	(drip? adj3 (nutrition$ or feed$ or fed$)).ti,ab.
32	or/21-31
33	*PRACTICE GUIDELINE/
34	guideline?.ti.
35	or/33-34
36	(standard$ adj3 protocol?).ti.
37	"European Society of Paediatric Gastroenterology, Hepatology and Nutrition".ti,ab.
38	ESPGHAN.ti,ab.
39	"European Society for Clinical Nutrition and Metabolism".ti,ab.
40	ESPEN.ti,ab.
41	"European Society of Paediatric Research".ti,ab.
42	ESPR.ti,ab.
43	"American Society for Parenteral and Enteral Nutrition".ti,ab.
44	ASPEN.ti,ab.
45	"British Association for Parenteral and Enteral Nutrition".ti,ab.
46	BAPEN.ti,ab.
47	"The Parenteral and Enteral Nutrition Group of the British Dietetic Association".ti,ab.
48	PENG.ti,ab.
49	"The British Society of Paediatric Gastroenterology, Hepatology and Nutrition".ti,ab.
50	BSPGHAN.ti,ab.
51	"National Nurses Nutrition Group".ti,ab.
52	NNNG.ti,ab.
53	"Patients on Intravenous and Nasogastric Nutrition Therapy".ti,ab.
54	PINNT.ti,ab.
55	"British Pharmaceutical Nutrition Group".ti,ab.
56	BPNG.ti,ab.
57	"British Association of Perinatal Medicine".ti,ab.

#	Searches
58	BAPM.ti,ab.
59	or/37-58
60	PRACTICE GUIDELINE/
61	guideline?.ti,ab.
62	or/60-61
63	(13 or 20) and 32 and 35
64	(13 or 20) and 32 and 36
65	(13 or 20) and 32 and 59 and 62
66	or/63-65
67	limit 66 to english language

Appendix C – Clinical evidence study selection

Clinical study selection for: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Figure 1: PRISMA flow chart of guideline selection for review question; general principles of parenteral nutrition



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Table 4: Clinical evidence table for RQ 9.1 general principles of neonatal parenteral nutrition (included guidelines only)

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Full citation Boullata JI, Gilbert K, Sacks G, et al. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. JPEN J Parenter Enteral Nutr. 2014; 38(3): 334-77. Ref Id 681445 Country where the study was carried out US Study type Clinical guideline Aim of the study To provide evidence-based guidance for clinical practices involving parenteral nutrition prescribing, order review, and preparation	Not reported	• Overall level of included minerals • Delivery of lipids via syringe or bags	*Scope and purpose (75%)* The overall objectives and health question were specifically described however the target population was unclear. *Stakeholder involvement (33%)* Clinical guideline authors represented a range of academic and clinical expertise. No patient or public representatives were included. The target audience was not clearly defined. *Rigour of development (49%)* No description of systematic methods. GRADE evaluation completed and evidence summaries included. Rationale is provided under each recommendation which considers the side effects and risks. Unclear if the guideline has been externally reviewed. *Clarity of presentation (81%)* Recommendations were easily identifiable, specific and unambiguous and some options for the management of the health issue were provided. *Applicability (23%)* No evidence of the consideration of barriers/facilitators to guideline implementation were located. *Editorial independence (50%)* Project described as unfunded. No information on conflicts of interest. Financial disclosures declared as none.

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Study dates Not reported			
Full citation Braegger, C., Bronsky, J., Cai, W., et al. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Fluid and electrolytes. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929357 Country where the study was carried out Europe Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition	Children aged 0-18 years (Recommendations are grouped into the following populations; Neonates during the transition phase (phase I), Neonates during intermediate phase (phase II), Neonates during the phase of stable growth (phase III), Children and infants beyond the neonatal period)	• Overall levels of blood and urinary electrolytes	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)*

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Study dates February 2015 until January 2018			Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full citation Braegger, C., Bronsky, J., Cai, W., Campoy, C., et al. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Iron and trace minerals. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929355 Country where the study was carried out Europe Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and	Children aged 0-18 years	• Overall level of included trace elements	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full citation Braegger, C., Bronsky, J., Cai, W., et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929354 Countries where the study was carried out Europe and China Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of	Children aged 0-18 years	• Overall levels of included vitamins	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities.

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			*Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full Citation Braegger, C., Bronsky, J., Cai, W., et al. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Complications. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929359 Country where the study was carried out Europe Study type Guideline Aim of the study The document is an update of previous guidelines	Children aged 0-18 years	• General practice for fluid volume • Overall levels of blood and urinary electrolytes • Filtration and protection from light	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)*

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full Citation Fusch, C., Bauer, K., Bohles, H. J., et al. Neonatology/Paediatrics - Guidelines on Parenteral Nutrition, Chapter 13. German medical science: GMS e-journal 2009;7: Doc 15. Ref Id 701386 Country where the study was carried out Germany Study type	Paediatric patients (including extremely premature infants up to teenagers weighing up to and over 100kg)	• Overall levels of included vitamins • General practice for fluid volume • Overall levels of blood and urinary electrolytes • Overall level of included trace elements	*Scope and purpose (61%)* The overall objectives of the guideline and population were specifically described. No specific health questions were outlined. *Stakeholder involvement (61%)* Information provided on working group members, however unclear if the views of patient or public representatives were sought. The target users of the guideline are professional groups involved in the application of parenteral nutrition and the document is intended to provide guidance to the medical and nursing profession on how to deal with specific situations. *Rigour of development (70%)* Systematic methods were used to search for the evidence. No specific inclusion/exclusion criteria are included however details of the databases, keywords, time periods and types of literature sought are described. Evaluation of the evidence of studies has taken place, and health benefits and side effects have been considered. There is no evidence of external review. The guideline will be updated if necessary five years after publication.

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Guideline Aim of the study To provide guidance for quality assurance for the practice of parenteral nutrition and to promote the heath and quality of life of patients Study dates Last quarter of 2007 until first quarter of 2009			*Clarity of presentation (83%)* Recommendations are specific and unambiguous and a description of the population appropriate to each recommendations are shown. Recommendations are separated into topics, and individual recommendations are separated with bullet points. *Applicability (35%)* No evidence that barriers or facilitators were considered. An implementation section is located in the introduction and methods chapter which includes a discussion of potential resource implications. *Editorial independence (88%)* The work was financially supported by the German Society for Nutritional Medicine as well as grants provided to the University of Munich Medical Center by Baxter Germany GmbH, Unterschleissheim, B. Braun Melsungen AG, Melsungen, and Fresenius Kabi Germany GmbH, Bad Homburg. The declarations of interest form is shown however no specific statement declaring conflicts of interest is included. Stated in the document that none of the experts working on the development of the guideline were either a representative or spokesperson for any particular company or range of products.
Full Citation Mihatsch, W., Picaud, J. C., Braegger, C., et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929450	Children aged 0-18 years	• Overall level of included minerals	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Countries where the study was carried out Europe and China Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full Citation Puntis, J. W. L., Braegger, C., Bronsky, J., et al. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Organisational aspects. Clinical Nutrition 2018; 37(6 Pt B): Ref Id	Children aged 0-18 years	• Delivery of lipids via syringe or bags • Filtration and protection from light	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public representatives were included. The target users of the guideline were described as health professionals.

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
929471 Country where the study was carried out Europe Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			*Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full Citation van den Akker, C. H. P., Braegger, C., Bronsky, J., et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition:	Children aged 0-18 years	• Delivery of lipids via syringe or bags • Filtration and protection from light	**Scope and purpose (56%)* The overall objectives of the guideline were specifically described, and health questions were at times addressed within the guideline document under the specific chapter. Target population could be deduced. *Stakeholder involvement (53%)* The guideline development group included global professionals with extensive experience managing parenteral nutrition. No patient or public

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
Lipids. Clinical Nutrition 2018; 37(6 Pt B) Ref Id 929511 Countries where the study was carried out Europe and China Study type Guideline Aim of the study The document is an update of previous guidelines produced in 2005 by ESPEN, ESPGHAN, ESPR together with CSPEN and is developed with the aim of providing up to date evidence for health professionals working with infants, children and adolescents receiving parenteral nutrition Study dates February 2015 until January 2018			representatives were included. The target users of the guideline were described as health professionals. *Rigour of development (71%)* Systematic literature searches via specified databases using described mesh and search terms were conducted and details of searches were clear and easy to locate in the document. The criteria for evidence selection was described, GRADE evaluation completed, and discussions of the benefits, side effects and risks of the relevant evidence were included. Unclear if an external review occurred but the chapter manuscripts were reviewed and edited by the project steering committee. No information provided on upcoming updates. *Clarity of presentation (92%)* Recommendations were easy to locate, numbered, in bold and in specific sections of the document. The different options for management of the conditions were provided for different age groups and severities. *Applicability (25%)* Some barriers are discussed within chapters however no tools or resources sought to facilitate application of the guideline. No economic evaluations have been described, but appears that some economic analysis has been sought from the evidence for specific chapters. *Editorial independence (50%)* Funding for the consensus conferences was provided by ESPGHAN, ESPEN, ESPR and CSPEN. No other funding was received, but support was provided by the Hungarian Cochrane organisation. Conflicts of interest are described as none. No statement that the funding did not influence the content of the guideline, nor described how conflicts of interest were sought.
Full Citation Vanek, Vincent W., Ayers, Phil, Kraft, Michael, Bouche, Jean M., et al. A call to action for optimizing the	Neonates, children and adults for various indications	• Overall levels of included vitamins • General practice for fluid volume	*Scope and purpose (64%)* The overall objectives of the guideline and health question were specifically described. The target population was unclear. *Stakeholder involvement (47%)*

Study details	Population	Topics covered	Notes on the quality assessment with AGREE II
electronic health record in the parenteral nutrition workflow. American journal of health-system pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists 2018; 75(18): 1400-1420. Ref Id 929513 Country where the study was carried out US Study type Consensus statement Aim of the study To outline some of the key challenges to prescribing, order review/verification, compounding and administration of parenteral nutrition using electronic health record systems and to publish a joint consensus statement on parenteral nutrition and electronic health record best practices. Study dates Work group formed in 2015		• Overall levels of blood and urinary electrolytes • Overall level of included trace elements	The guideline development group included individuals from relevant professional groups. Did not appear to include patient or public representatives. The goals of the work group are specified however the intended guideline audience was unclear. *Rigour of development (27%)* No description of systematic methods, evidence selection or strengths/limitations of the evidence are provided. Information on the methods are provided and discussions of risks and benefits are evident in the text. Recommendations are located in separate tables with no explicit link to the evidence. It is unclear whether the guideline has been externally reviewed and no procedure for updating the guideline is detailed. *Clarity of presentation (86%)* Recommendations are specific and unambiguous and different options relevant to the associated population are provided. Key recommendations are easily identified in the table and grouped together. *Applicability (48%)* It is unclear whether the facilitators and barriers were considered. Tools and their instructions for use are provided to facilitate application of the guideline. No evidence of economic evaluations *Editorial independence (71%)* Statements are provided that there was no funding to disclose, nor any potential conflicts of interest provided by the authors. It is not described how the conflicts of interest were sought.

CSPEN: Chinese Society of Parenteral and Enteral Nutrition; ESPEN: European Society for Clinical Nutrition and Metabolism; ESPHGAN: European Society of Paediatric Gastroenterology, Hepatology and Nutrition; ESPR: European Society of Paediatric Research; GRADE: Grading of Recommendations Assessment, Development and Evaluation.
**Guidelines published by ESPGHAN, ESPEN and ESPR, and those by ESPGHAN, ESPEN, ESPR and CSPEN were assessed under one AGREE II appraisal as they were developed using the same methods*

Appendix E – Forest plots

Forest plots for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Forest plots are not appropriate for formal consensus.

Appendix F – AGREE II tables

Appraisal of Guideline Research and Evaluation version 2 (AGREE II) tables for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Table 5: AGREE II quality assessment of all identified guidelines (including those later excluded due to poor quality)

		Domains							
Guideline reference	**Year**	Scope and purpose %	Stakeholder involvement %	Rigour of development %	Clarity of presentation %	Applicability %	Editorial independence %	Overall score	Included/ excluded
Ben 2008 Nutritional management of newborn infants: Practical guidelines. World Journal of Gastroenterology; 14: 6133-6139.	2008	56	6	27	72	23	0	25	Excluded
Boullata 2014 A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing.JPEN J Parenter Enteral Nutr.; 38(3): 334-77.	2014	75	33	49	81	23	50	83	Included
British Association of Perinatal Medicine 2016 The Provision of Parenteral Nutrition within Neonatal Services - A Framework for Practice. 2016.	2016	61	50	19	78	42	0	50	Excluded
Cai 2013 Working Group Of Pediatrics Chinese Society Of Parenteral And Enteral Nutrition, Working Group Of Neonatology Chinese Society Of Pediatrics, Working Group Of Neonatal Surgery Chinese Society Of Pediatric Surgery. CSPEN guidelines for	2013	58	25	25	81	31	46	42	Excluded

		Domains							
Guideline reference	**Year**	Scope and purpose %	Stakeholder involvement %	Rigour of development %	Clarity of presentation %	Applicability %	Editorial independence %	Overall score	Included/ excluded
nutrition support in neonates. Asia Pac J Clin Nutr.; 22(4): 655-63.									
Fusch 2009 Neonatology/Paediatrics - Guidelines on Parenteral Nutrition, Chapter 13. Ger Med Sci.;7: Doc15.	2009	61	61	70	83	35	88	75	Included
Health Services Executive and Royal College of Physicians of Ireland 2017 Guideline on the Use of Parenteral Nutrition in Neonatal and Paediatric Units.	2017	69	58	29	78	48	8	25	Excluded
NHS East of England Perinatal Network 2015 Clinical Guideline: Parenteral Feeding of Infants on the Neonatal Unit. 2015	2015	56	56	23	81	56	0	33	Excluded
Bregger 2018a, 2018b, 2018c, 2018d, Putis 2018, Mihatsch 2019, ven den Akker 2018 ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition Clin Nutr; 37(6 Pt B)	2018	56	53	71	92	25	50	75	Included (n =7 separate topics in this guideline are published individuall y by same or different authors but all developed

		Domains							
Guideline reference	**Year**	Scope and purpose %	Stakeholder involvement %	Rigour of development %	Clarity of presentation %	Applicability %	Editorial independence %	Overall score	Included/ excluded
									using the same methods)*
Sydney Local Health District 2018 Guideline. Women and Babies: Newborn parenteral nutrition.	2018	53	22	36	75	46	0	42	Excluded
Vanek 2018A call to action for optimizing the electronic health record in the parenteral nutrition workflow. Am J Health Syst Pharm.; 75(18): 1400-1420.	2018	64	47	27	86	48	71	58	Included
Vanek 2012 A.S.P.E.N. position paper: recommendations for changes in commercially available parenteral multivitamin and multi-trace element products. Nutr Clin Pract.; 27(4): 440-91.	2012	64	33	34	81	40	33	58	Excluded
Western Australia Women and Newborn Health Service 2016 Parenteral Nutrition. 2016.	2016	28	17	9	25	23	0	8	Excluded

CSPEN: Chinese Society of Parenteral and Enteral Nutrition; ESPEN: European Society for Clinical Nutrition and Metabolism; ESPHGAN: European Society of Paediatric Gastroenterology, Hepatology and Nutrition; ESPR: European Society of Paediatric Research; GRADE: Grading of Recommendations Assessment, Development and Evaluation.
**Guidelines published by ESPGHAN, ESPEN and ESPR, and those by ESPGHAN, ESPEN, ESPR and CSPEN were assessed under one AGREE II appraisal as they were developed using the same methods*

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

One global search was conducted for this review question. See supplementary material D for further information.

Appendix H – Economic evidence tables

Economic evidence tables for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

No economic evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

No economic evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Clinical studies

Guidelines that were considered for inclusion but did not meet pre-specified quality criteria when the AGREE II tool was applied are shown in bold font.

Table 6: Excluded studies and reasons for their exclusion

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
A. S. P. E. N. Clinical Practice Committee Shortage Subcommittee, Plogsted S, Brooks G. DiBaise J. Fuhrman T. Ybarra J. Holcombe B. Andris D. A. Houston D. R. Plogsted S. W., A.S.P.E.N. parenteral nutrition trace element product shortage considerations, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 29, 249-51, 2014	Guideline does not match eligibility criteria. Recommendations checked; made regarding trace element shortage considerations only. This does not match the area of interest specified in the protocol.
Abu-El-Haija, Maisam, Uc, Aliye, Werlin, Steven L., Freeman, A. Jay, Georgieva, Miglena, Pavkov, Danijela Jojkic, Kalnins, Daina, Kochavi, Brigitte, Koot, Bart G. P., Van Biervliet, Stephanie, Walkowiak, Jaroslaw, Wilschanski, Michael, Morinville, Veronique D., Nutritional Considerations in Pediatric Pancreatitis: A Position Paper from the NASPGHAN Pancreas Committee, ESPGHAN Pancreas Working Group, Journal of Pediatric Gastroenterology and Nutrition, 2018	Guideline does not match eligibility criteria. Recommendations checked; for patients with pancreatitis only, not in the areas of interest specified in the protocol.
Abu-El-Haija, Maisam, Uc, Aliye, Werlin, Steven L., Freeman, Alvin Jay, Georgieva, Miglena, Jojkic-Pavkov, Danijela, Kalnins, Daina, Kochavi, Brigitte, Koot, Bart G. P., Van Biervliet, Stephanie, Walkowiak, Jaroslaw, Wilschanski, Michael, Morinville, Veronique D., Nutritional Considerations in Pediatric Pancreatitis: A Position Paper from the NASPHAN Pancreas Committee and ESPHAN Cystic Fibrosis/Pancreas Working Group, Journal of Pediatric Gastroenterology and Nutrition, 67, 131-143, 2018	Guideline does not match eligibility criteria. Recommendations checked; for patients with pancreatitis only, not in the areas of interest specified in the protocol.
Al-Rafay, Safy S., Al-Sharkawy, Sabah S., Educational outcomes associated with providing a comprehensive guidelines program about nursing care of preterm neonates receiving total parenteral nutrition, Clinical nursing research, 21, 142-58, 2012	Does not match eligibility criteria. Study assesses educational outcomes of Neonatal Intensive Care Unit (NICU) nurses.
Arsenault, D., Brenn, M., Kim, S., Gura, K., Compher, C., Simpser, E., Puder, M., A.S.P.E.N. clinical guidelines: Hyperglycemia and hypoglycemia in the neonate receiving parenteral nutrition, Journal of Parenteral and Enteral Nutrition, 36, 81-95, 2012	Does not match eligibility criteria. The guideline reports recommendations on hyperglycaemia and hypoglycaemia only which are not areas of interest specified in the protocol.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Ayers, P., Adams, S., Boullata, J., Gervasio, J., Holcombe, B., Kraft, M. D., Marshall, N., Neal, A., Sacks, G., Seres, D. S., Worthington, P., Guenter, P., A.S.P.E.N. Parenteral nutrition safety consensus recommendations, Journal of Parenteral and Enteral Nutrition, 38, 296-333, 2014	Does not match eligibility criteria. Recommendations checked; the guideline does not make recommendations in the areas of interest specified in the protocol.
Becker, Patricia J., Nieman Carney, Liesje, Corkins, Mark Richard, Monczka, Jessica, Smith, Elizabeth, Smith, Susan Elizabeth, Spear, Bonnie A., White, Jane V., Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition), Journal of the Academy of Nutrition and Dietetics, 114, 1988-2000, 2014	Does not match eligibility criteria. Recommendations made only for paediatric population aged 1 month to 18 years.
Becker, Patricia, Carney, Liesje Nieman, Corkins, Mark R., Monczka, Jessica, Smith, Elizabeth, Smith, Susan E., Spear, Bonnie A., White, Jane V., Academy of, Nutrition, Dietetics,, American Society for, Parenteral, Enteral, Nutrition, Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition), Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 30, 147-61, 2015	Does not match eligibility criteria. The included population is children aged 1 month to 18 years. Recommendations are made on undernutrition and do not match areas of interest specified in the protocol.
Ben, X. M., Nutritional management of newborn infants: Practical guidelines, World Journal of Gastroenterology, 14, 6133-6139, 2008	**Single author. Unclear whether guideline is national or local. The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 56%; stakeholder involvement: 6%; rigour of development: 27%; clarity of presentation: 72%; applicability: 23%; editorial independence: 0%.**
Bodeur, Cynthia, Aucoin, Julia, Johnson, Raeanne, Garrison, Kaitlyn, Summers, Amanda, Schutz, Kristen, Davis, Megan, Woody, Sherri, Ellington, Kelly, Clinical practice guidelines--Nursing management for pediatric patients with small bowel or multivisceral transplant, Journal for specialists in pediatric nursing : JSPN, 19, 90-100, 2014	Does not match eligibility criteria. Recommendations checked; for paediatric patients with transplant only.
Bolisetty S, Osborn D, Sinn J, Lui K; Australasian Neonatal Parenteral Nutrition Consensus Group. Standardised neonatal parenteral nutrition formulations - an Australasian group consensus 2012. BMC Pediatr. 2014 Feb 18; 14:48.	Does not meet eligibility criteria. Paper is a consensus document, not a guideline. Consensus is utilised to determine agreement on standardised parenteral formulations for use in neonatal intensive care units in Australia and New Zealand. Agreed formulations are stated in the topic areas of interest (as specified in the

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
	protocol) however these statements are not described as guidelines nor recommendations in the document.
Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Energy, Clinical Nutrition, 2018	Does not meet eligibility criteria. Recommendations checked; do not match the areas of interest specified in the protocol.
Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Carbohydrates, Clinical Nutrition, 2018	The guideline does not meet the eligibility criteria. It does not report recommendations on the areas of interest as specified in the protocol.
British Association of Perinatal Medicine, The Provision of Parenteral Nutrition within Neonatal Services - A Framework for Practice, 2016	**The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 61%; stakeholder involvement: 50%; rigour of development: 19%; clarity of presentation: 78%; applicability: 42%; editorial independence: 0%.**
Cai, W., CSPEN guidelines for nutrition support in neonates, Asia Pacific Journal of Clinical Nutrition, 22, 655-663, 2013	**The guideline does not match the eligibility criteria. it was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 58%; stakeholder involvement: 25%; rigour of development: 25%; clarity of presentation: 81%; applicability: 31%; editorial independence: 46%.**

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Callan, J., Salvestrini, C., Parenteral Nutrition in paediatrics, Paediatrics and Child Health (United Kingdom), 23, 356-361, 2013	Does not match eligibility criteria. The paper describes those recommendations already made by ESPGHAN/ ESPEN in addition to those in place in the authors' centre (local guideline only).
Castellani, C., Duff, A. J. A., Bell, S. C., Heijerman, H. G. M., Munck, A., Ratjen, F., Sermet-Gaudelus, I., Southern, K. W., Barben, J., Flume, P. A., Hodkova, P., Kashirskaya, N., Kirszenbaum, M. N., Madge, S., Oxley, H., Plant, B., Schwarzenberg, S. J., Smyth, A. R., Taccetti, G., Wagner, T. O. F., Wolfe, S. P., Drevinek, P., ECFS best practice guidelines: the 2018 revision, Journal of Cystic Fibrosis, 17, 153-178, 2018	Does not match eligibility criteria. Recommendations checked; for cystic fibrosis only.
Compher, C. W., Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients, 2009, Journal of Parenteral and Enteral Nutrition, 33, 255-259, 2009	Does not match eligibility criteria. Development document; no recommendations are made.
Corkins, Mark R., Griggs, Kathleen C., Groh-Wargo, Sharon, Han-Markey, Theresa L., Helms, Richard A., Muir, Linda V., Szeszycki, Elaina E., Task Force on Standards for Nutrition Support: Pediatric Hospitalized, Patients, American Society for, Parenteral, Enteral Nutrition Board of, Directors, American Society for, Parenteral, Enteral, Nutrition, Standards for nutrition support: pediatric hospitalized patients, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 28, 263-76, 2013	Document is described as "standards of practice which should define the structure needed to provide competent care". Document is not specifically a guideline and no relevant recommendations matching the topics of interest for neonates were located.
Corkins, Mark R., Guenter, Peggi, DiMaria-Ghalili, Rose Ann, Jensen, Gordon L., Malone, Ainsley, Miller, Sarah, Patel, Vihas, Plogsted, Steve, Resnick, Helaine E., American Society for, Parenteral, Enteral, Nutrition, A.S.P.E.N. data brief 2014: use of enteral and parenteral nutrition in hospitalized patients with a diagnosis of malnutrition: United States, 2010, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 29, 698-700, 2014	Does not match eligibility criteria. Not a guideline (report only).
De Hoog, B., Gjessing, P., Henfridsson, P., Holmboe, C., Larsen, L., Merras-Salmio, L., Rasmussen, I., Ellegard, L., Rasmussen, H., The nordic nutrition Academy's pocket guide to parenteral nutrition, Clinical Nutrition, Supplement, 6, 93, 2011	Abstract only.
Druyan, M. E., Compher, C., Boullata, J. I., Braunschweig, C. L., George, D. E., Simpser, E., Worthington, P. A., Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: Applying the GRADE system to development of A.S.P.E.N. clinical guidelines, Journal of Parenteral and Enteral Nutrition, 36, 77-80, 2012	Does not match eligibility criteria. Not a guideline. A report on applying GRADE to ASPEN guidelines.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Espinosa Fernandez, Maria Gracia, Sanchez-Tamayo, Tomas, Moreno Algarra, Maria C., Fernandez Romero, Veronica, Vallejo Triano, Jose, Tapia Moreno, Elias, Salguero Garcia, Enrique, New clinical practice guideline on enteral feeding in very low birth weight infants; second part, Nutricion hospitalaria, 30, 329-37, 2014	Does not match eligibility criteria. Guideline makes recommendations on enteral feeding only.
Fallon, E. M., Nehra, D., Potemkin, A. K., Gura, K. M., Simpser, E., Compher, C., Puder, M., A.S.P.E.N. clinical guidelines: Nutrition support of neonatal patients at risk for necrotizing enterocolitis, Journal of Parenteral and Enteral Nutrition, 36, 506-523, 2012	Does not match eligibility criteria. Guideline does not make any recommendations matching the areas of interest specified in the protocol.
Fawaz, Rima, Baumann, Ulrich, Ekong, Udeme, Fischler, Bjorn, Hadzic, Nedim, Mack, Cara L., McLin, Valerie A., Molleston, Jean P., Neimark, Ezequiel, Ng, Vicky L., Karpen, Saul J., Guideline for the Evaluation of Cholestatic Jaundice in Infants: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition, Journal of pediatric gastroenterology and nutrition, 64, 154-168, 2017	Does not match eligibility criteria. Recommendations are made on the evaluation of cholestatic jaundice only. No recommendations on the relevant areas of interest specified in the protocol.
Forbes, Alastair, Escher, Johanna, Hebuterne, Xavier, Klek, Stanislaw, Krznaric, Zeljko, Schneider, Stephane, Shamir, Raanan, Stardelova, Kalina, Wierdsma, Nicolette, Wiskin, Anthony E., Bischoff, Stephan C., ESPEN guideline: Clinical nutrition in inflammatory bowel disease, Clinical nutrition (Edinburgh, Scotland), 36, 321-347, 2017	Does not match eligibility criteria. Recommendations are made on inflammatory bowel disease only.
Great Ormond Street Hospital, Nutrition: parenteral, 2015	The guideline does not match eligibility criteria. Local guideline only.
Guarino, Alfredo, Ashkenazi, Shai, Gendrel, Dominique, Lo Vecchio, Andrea, Shamir, Raanan, Szajewska, Hania, European Society for Pediatric Gastroenterology, Hepatology, Nutrition,, European Society for Pediatric Infectious, Diseases, European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014, Journal of pediatric gastroenterology and nutrition, 59, 132-52, 2014	Does not match eligibility criteria. Recommendations are made on the management of gastroenteritis, not in the areas of interest specified in the protocol.
Hay, W. W., Optimizing nutrition of the preterm infant, Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics, 19, 1-21, 2017	Does not match eligibility criteria. Recommendations are not associated to a national or regional institution, appears to be a local guideline only.
Health Services Executive and Royal College of Physicians of Ireland, Guideline on the Use	**The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria**

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
of Parenteral Nutrition in Neonatal and Paediatric Units, 2017	**of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 69%; stakeholder involvement: 58%; rigour of development: 29%; clarity of presentation: 78%; applicability: 48%; editorial independence: 8%.**
Holick,M.F., The D-lightful vitamin D for child health, JPEN, 36, 9S-19S, 2012	Does not match eligibility criteria. This is a report on recommendations on Vitamin D and does not include areas of interest specified in the protocol.
Iacobelli, S., Bonsante, F., Gouyon, J. B., Fluid and electrolyte intake during the first week of life in preterm infants receiving parenteral nutrition according current guidelines, Minerva pediatrica, 62, 203-4, 2010	No full text available.
Imam, A., Haque, K. N., Guideline for management of neonatal Necrotising Enterocolitis in resource limited countries, Pakistan Paediatric Journal, 36, 180-191, 2012	Does not match eligibility criteria. No relevant recommendations are made according to the areas of interest specified in the protocol.
Jaksic, T., Hull, M. A., Modi, B. P., Ching, Y. A., George, D., Compher, C., A.S.P.E.N. clinical guidelines: Nutrition support of neonates supported with extracorporeal membrane oxygenation, Journal of Parenteral and Enteral Nutrition, 34, 247-253, 2010	Does not match eligibility criteria. No recommendations are made on the areas of interest specified in the protocol.
Johnsen, Jacob Clarke, Reese, Susan Anne, Mackay, Mark, Anderson, Collin R., Jackson, Daniel, Paul, Irasema Libertad, Assessing Selenium, Manganese, and Iodine Status in Pediatric Patients Receiving Parenteral Nutrition, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 32, 552-556, 2017	Does not match eligibility criteria. Review, not a guideline.
Karpen, Heidi E., Nutrition in the Cardiac Newborns: Evidence-based Nutrition Guidelines for Cardiac Newborns, Clinics in perinatology, 43, 131-45, 2016	Does not match eligibility criteria. Recommendations for cardiac newborns, not on the areas of interest specified in the protocol.
Koletzko, B., Hunt, J., Krohn, K., Shamir, R., Agostoni, C., Ball, P., Carnielli, V., Chaloner, C., Clayton, J., Colomb, V., Dijsselhof, M., Fusch, C., Gandullia, P., Genzel-Boroviczeny, O., Gottrand, F., Goulet, O., Granot, E., Gray, J., Guerra, A., Hill, S., Holden, C., Horn, V., Jago, L., Jochum, F., Kolacek, S., Koletzko, S., Ksiazyk, J., Lapillonne, A., Luukkainen, P., Lyszkowska, M., MacDonald, S., Mestroviae, J., Mihatsch, W., Milla, P., Mimouni, F., Misak, Z., Mrsic, I., Newby, L., Pohlandt, F., Protheroe, S., Puntis, J., Rigo, J., Riskin, A., Roberts, J., Szitanyi, P., Thomas, A., Vaisman, N., van Goudoever, H., Yaron, A., Report on the guidelines on parenteral nutrition in infants, children and adolescents, Clinical Nutrition, 24, 1105-1109, 2005	Does not match eligibility criteria. Paper is a report, not a guideline.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Lacaille, Florence, Gupte, Girish, Colomb, Virginie, D'Antiga, Lorenzo, Hartman, Corina, Hojsak, Iva, Kolacek, Sanja, Puntis, John, Shamir, Raanan, Espghan Working Group of Intestinal Failure, Intestinal, Transplantation, Intestinal failure-associated liver disease: a position paper of the ESPGHAN Working Group of Intestinal Failure and Intestinal Transplantation, Journal of Pediatric Gastroenterology and Nutrition, 60, 272-83, 2015	Does not match eligibility criteria. No recommendations are made in the areas of interest specified in the protocol.
Mangili, G., Garzoli, E., Sadou, Y., Feeding dysfunctions and failure to thrive in neonates with congenital heart diseases, Pediatria Medica e Chirurgica, 40, 1-4, 2018	Does not match eligibility criteria. Paper is a review, not a guideline.
McGrory, C. H., Ondeck-Williams, M., Hilburt, N., Constantinescu, S., Silva, P., Daller, J. A., Coscia, L. A., Armenti, V. T., Nutrition, pregnancy, and transplantation, Nutrition in Clinical Practice, 22, 512-516, 2007	Does not match eligibility criteria. Recommendations checked; no relevant recommendations matching the areas of interest specified in the protocol.
Mehta, Nilesh M., Skillman, Heather E., Irving, Sharon Y., Coss-Bu, Jorge A., Vermilyea, Sarah, Farrington, Elizabeth Anne, McKeever, Liam, Hall, Amber M., Goday, Praveen S., Braunschweig, Carol, Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition, JPEN. Journal of parenteral and enteral nutrition, 148607117711387, 2017	Does not match eligibility criteria. Included population is critically ill patients between 1 month and 18 years of age. No relevant recommendations are made according to the areas of interest specified in the protocol.
Mehta,N.M., Approach to enteral feeding in the PICU, Nutrition in Clinical Practice, 24, 377-387, 2009	Does not match eligibility criteria. Recommendations on enteral feeding only.
Meyer, R., Meike, T., Hegi, L., Ettel, E., Furlano, R., Schulzke, S., Developing and implementing standard parenteral nutrition solutions for a neonatal unit, Intensive Care Medicine, 37, S394, 2011	Abstract only.
Mihatsch, W., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Dirk, V., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Guideline development process for the updated guidelines, Clinical Nutrition, 2018	This is the development document for ESPGHAN/ESPEN/ESPR/CSPEN 2018 guidelines. Does not match eligibility criteria for inclusion as no recommendations are made. The document was used in conjunction with ESPGHAN/ESPEN/ESPR/CSPEN 2018 guidelines on individual topics for appraisal with AGREE II.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Monagle,P., Chan,A.K.C., Goldenberg,N.A., Ichord,R.N., Journeycake,J.M., Nowak-Gottl,U., Vesely,S.K., Antithrombotic therapy in neonates and children: Antithrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines, Chest, 141, e737S-e801S, 2012	Does not match eligibility criteria. No recommendations made on the areas of interest specified in the protocol.
Mouzaki, M., Ng, V., Kamath, B. M., Selzner, N., Pencharz, P., Ling, S. C., Enteral energy and macronutrients in end-stage liver disease, Jpen: Journal of Parenteral & Enteral Nutrition, 38, 673-81, 2014	Does not match eligibility criteria. No relevant recommendations are made according to the areas of interest specified in the protocol.
Nehra,D., Carlson,S.J., Fallon,E.M., Kalish,B., Potemkin,A.K., Gura,K.M., Simpser,E., Compher,C., Puder,M., A.S.P.E.N. clinical guidelines: Nutrition support of neonatal patients at risk for metabolic bone disease, Journal of Parenteral and Enteral Nutrition, 37, 570-578, 2013	Recommendations for vitamin D are provided for breastfed infants only. This population does not match that specified in the protocol. Guideline does not match eligibility criteria.
NHS Ashford and St. Peter's Hospitals, Parenteral Nutrition for Neonates, 2012	Guideline does not match eligibility criteria. Local guideline only.
NHS Ashford and St. Peter's Hospitals, Neonatal Unit Nutrition and Feeding Guidelines, 2012	Guideline does not match eligibility criteria. Local guideline only.
NHS East of England Perinatal Network, Clinical Guideline: Parenteral Feeding of Infants on the Neonatal Unit, 2015	**Regional guideline. The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 56%; stakeholder involvement: 56%; rigour of development: 23%; clarity of presentation: 81%; applicability: 56%; editorial independence: 0%.**
NHS Pharmaceutical Quality Assurance Committee, A standard protocol for derivation and assessment of stability. Part 4 - parenteral nutrition, 2016	Does not match eligibility criteria. The document is a standard protocol (not a guideline) and recommendations are made on the derivation and assessment of stability of parenteral nutrition.
NHS Royal Cornwall Hospitals, Standardised concentrated neonatal parenteral nutrition, 2018	Guideline does not match eligibility criteria. Local guideline only.
NHS Worcestershire, Guideline for the prescription of parenteral nutrition (PN) on the neonatal unit, 2015	Guideline does not match eligibility criteria. Local guideline only.
Nishida, O., Ogura, H., Egi, M., Fujishima, S., Hayashi, Y., Iba, T., Imaizumi, H., Inoue, S., Kakihana, Y., Kotani, J., Kushimoto, S., Masuda, Y., Matsuda, N., Matsushima, A., Nakada, T. A., Nakagawa, S., Nunomiya, S., Sadahiro, T., Shime, N., Yatabe, T., Hara, Y., Hayashida, K., Kondo, Y., Sumi, Y., Yasuda, H., Aoyama, K., Azuhata, T., Doi, K., Doi, M., Fujimura, N., Fuke, R., Fukuda, T., Goto, K., Hasegawa, R., Hashimoto, S., Hatakeyama, J., Hayakawa, M., Hifumi, T., Higashibeppu, N., Hirai, K., Hirose, T., Ide, K., Kaizuka, Y., Kan'o, T., Kawasaki, T., Kuroda, H., Matsuda, A., Matsumoto, S., Nagae,	Guidelines for paediatric and adult patients presenting with confirmed or suspected sepsis or septic shock. Does not match the population or areas of interest as specified in the protocol eligibility criteria.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
M., Onodera, M., Ohnuma, T., Oshima, K., Saito, N., Sakamoto, S., Sakuraya, M., Sasano, M., Sato, N., Sawamura, A., Shimizu, K., Shirai, K., Takei, T., Takeuchi, M., Takimoto, K., Taniguchi, T., Tatsumi, H., Tsuruta, R., Yama, N., Yamakawa, K., Yamashita, C., Yamashita, K., Yoshida, T., Tanaka, H., Oda, S., The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016 (J-SSCG 2016), Acute Medicine and Surgery, 5, 3-89, 2018	
Nottingham Children's Hospital, Neonatal Parenteral Nutrition (PN), 2017	Guideline does not match eligibility criteria. Local guideline only.
Paediatric Chief Pharmacists Group, Improving practice and reducing risk in the provision of parenteral nutrition for neonates and children: Report of the Paediatric Chief Pharmacists Group, 2011	Does not match eligibility criteria. The report provides recommendations on the minimum pathway of care standards for parenteral nutrition. Does not include recommendations on the areas of interest.
Pediatric Gastroenterology Chapter of Indian Academy of, Pediatrics, Bhatia, Vidyut, Bavdekar, Ashish, Yachha, Surender Kumar, Indian Academy of, Pediatrics, Management of acute liver failure in infants and children: consensus statement of the pediatric gastroenterology chapter, Indian academy of pediatrics, Indian Pediatrics, 50, 477-82, 2013	No relevant recommendations match the areas of interest specified in the protocol. Guideline for management of acute liver failure in India.
Picaud, J. C., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Standard versus individualized parenteral nutrition, Clinical Nutrition, 2018	The guideline does not match the eligibility criteria. Does not provide recommendations on the areas of interest specified in the protocol. Recommendations are made on standardised vs individualised bags which has been covered by an evidence review.
Puntis, J. W. L., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W.,	The guideline does not match eligibility criteria. It does not provide recommendations on the areas of interest specified in the protocol.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Venous access, Clinical Nutrition, 2018	
Raiten, D. J., Steiber, A. L., Carlson, S. E., Griffin, I., Anderson, D., Hay, W. W., Robins, S., Neu, J., Georgieff, M. K., Groh-Wargo, S., Fenton, T. R., Working group reports: Evaluation of the evidence to support practice guidelines for nutritional care of preterm infants-the Pre-B Project, American Journal of Clinical Nutrition, 103, 648S-678S, 2016	Not a guideline.
Raiten, Daniel J., Steiber, Alison L., Hand, Rosa K., Executive summary: evaluation of the evidence to support practice guidelines for nutritional care of preterm infants-the Pre-B Project, The American journal of clinical nutrition, 103, 599S-605S, 2016	Not a guideline.
S. ENPE's standardization group, Pedron Giner, C., Martinez-Costa, C., Navas-Lopez, V. M., Gomez-Lopez, L., Redecillas-Ferrero, S., Moreno-Villares, J. M., Benlloch-Sanchez, C., Blasco-Alonso, J., Garcia-Alcolea, B., Gomez-Fernandez, B., Ladero-Morales, M., Morais-Lopez, A., Rosell Camps, A., Consensus on paediatric enteral nutrition access: a document approved by SENPE/SEGHNP/ANECIPN/SECP, Nutricion hospitalaria, 26, 1-15, 2011	Guideline includes recommendations for enteral feeding only. Therefore does not match eligibility criteria.
Sabery, N., Duggan, C., A.S.P.E.N. clinical guidelines: Nutrition support of children with human immunodeficiency virus infection, Journal of Parenteral and Enteral Nutrition, 33, 588-606, 2009	Recommendations are for children with human immunodeficiency virus infection. Does not match the population specified in the eligibility criteria.
Sainz de Pipaon, M., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker, C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: Amino acids, Clinical Nutrition, 2018	The guideline does not match eligibility criteria. Recommendations are not provided in the areas of interest specified in the protocol. Amino acids have already been covered by an evidence review.
Sanchez-Tamayo, Tomas, Espinosa Fernandez, Maria G., Moreno Algarra, Maria C., Fernandez Romero, Veronica, Vallejo Triano, Jose, Tapia Moreno, Elias, Salguero Garcia, Enrique, New clinical practice guideline on enteral feeding in very low birth weight infants; first part, Nutricion hospitalaria, 30, 321-8, 2014	No relevant recommendations to the areas of interest specified in the protocol. The guideline is for enteral feeding.

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
Shores, D., Bullard, J., Stewart, D., Haney, C., Tymann, H., Schwarz, K., Implementation of feeding guidelines for infants with intestinal abnormalities requiring surgical intervention, Clinical and Translational Science, 7, 257, 2014	Abstract only.
SickKids, Guidelines for the Administration of Enteral and Parenteral Nutrition in Paediatrics, 2007	Does not match eligibility criteria - published prior to January 2008
Sion-Sarid, Racheli, Cohen, Jonathan, Houri, Zion, Singer, Pierre, Indirect calorimetry: a guide for optimizing nutritional support in the critically ill child, Nutrition (Burbank, Los Angeles County, Calif.), 29, 1094-9, 2013	Review, not a guideline.
Stein, J., Boehles, H. J., Blumenstein, I., Goeters, C., Schulz, R., Amino acids - Guidelines on Parenteral Nutrition, Chapter 4, German medical science : GMS e-journal, 7, 2009	Guideline does not match eligibility criteria. Recommendations on amino acids for adults. Not the population or areas of interest specified in the protocol.
Stevenson, D. K., Bhutani, V. K., Preterm Neonates: Beyond the Guidelines for Neonatal Hyperbilirubinemia, Clinics in Perinatology, 43, 2016	Preface, not a guideline.
Sweet, D., European guidelines for the management of RDS-2013 update, Journal of Perinatal Medicine. Conference: 11th World Congress of Perinatal Medicine, 41, 2013	Abstract only.
Sweet,D.G., Carnielli,V., Greisen,G., Hallman,M., Ozek,E., Plavka,R., Saugstad,O.D., Simeoni,U., Speer,C.P., Halliday,H.L., European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants - 2010 update, Neonatology, 97, 402-417, 2010	No recommendations on the areas of interest specified in the protocol. Recommendation on the management of neonatal respiratory distress syndrome in preterm infants. Does not match eligibility criteria.
Sydney Local Health District, Guideline. Women and Babies: Newborn parenteral nutrition, 2018	**The author is specified as Sydney Local Health District (therefore local guideline) however the consensus group comprised NICUs from Australia, NZ, Malaysia, Singapore and India. The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 53%; stakeholder involvement: 22%; rigour of development: 36%; clarity of presentation: 75%; applicability: 46%; editorial independence: 0%.**
Tabbers, M., Braegger, C., Bronsky, J., Cai, W., Campoy, C., Carnielli, V., Darmaun, D., Decsi, T., Domellof, M., Embleton, N., Fewtrell, M., Fidler Mis, N., Franz, A., Goulet, O., Hartman, C., Hill, S., Hojsak, I., Iacobelli, S., Jochum, F., Joosten, K., Kolacek, S., Koletzko, B., Ksiazyk, J., Lapillonne, A., Lohner, S., Mesotten, D., Mihalyi, K., Mihatsch, W. A., Mimouni, F., Molgaard, C., Moltu, S. J., Nomayo, A., Picaud, J. C., Prell, C., Puntis, J., Riskin, A., Saenz De Pipaon, M., Senterre, T., Shamir, R., Simchowitz, V., Szitanyi, P., Tabbers, M. M., Van Den Akker,	The guideline does not match eligibility criteria. Recommendations are not provided in the areas of interest specified in the protocol (recommendations on home parenteral nutrition only).

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
C. H. B., Van Goudoever, J. B., Van Kempen, A., Verbruggen, S., Wu, J., Yan, W., ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Home parenteral nutrition, Clinical Nutrition, 2018	
Teitelbaum, Daniel H., Guenter, Peggi, Griebel, Donna, Abrams, Steven A., Bark, Staffan, Baker, Mary, Berry, Karyn L., Bistrian, Bruce R., Brenna, J. Thomas, Bonnot, Denis, Carpentier, Yvon A., Deckelbaum, Richard J., Hise, Mary, Koletzko, Berthold, Mirtallo, Jay M., Mulberg, Andrew E., O'Reilly, Randall C., Shaffer, Jonathan, von Kleist, Elke, Zaloga, Gary P., Ziegler, Thomas R., Proceedings From FDA/A.S.P.E.N. Public Workshop: Clinical Trial Design for Intravenous Fat Emulsion Products, October 29, 2013, JPEN. Journal of parenteral and enteral nutrition, 39, 768-86, 2015	Not a guideline.
UCSF Children's Hospital, Neonatal Parenteral Nutrition, 2006	Guideline does not match eligibility criteria. Manual providing recommendations on neonatal parenteral nutrition for the University of California Children's Hospital. Local guideline.
Vanek, Vincent W., Borum, Peggy, Buchman, Alan, Fessler, Theresa A., Howard, Lyn, Jeejeebhoy, Khursheed, Kochevar, Marty, Shenkin, Alan, Valentine, Christina J., Novel Nutrient Task Force, Parenteral Multi-Vitamin, Multi-Trace Element Working, Group, American Society for, Parenteral, Enteral Nutrition Board of, Directors, A.S.P.E.N. position paper: recommendations for changes in commercially available parenteral multivitamin and multi-trace element products, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 27, 440-91, 2012	**The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 64%; stakeholder involvement: 33%; rigour of development: 34%; clarity of presentation: 81%; applicability: 40%; editorial independence: 33%.**
Vanek, Vincent W., Borum, Peggy, Buchman, Alan, Fessler, Theresa A., Howard, Lyn, Shenkin, Alan, Valentine, Christina J., Novel Nutrient Task Force, Parenteral Vitamin, Trace Element Working, Group, the American Society for, Parenteral, Enteral, Nutrition, Novel Nutrient Task Force Parenteral, Vitamin, Trace Element Working, Group, the American Society for, Parenteral, Enteral Nutrition, A. S. P. E. N., Vanek Vw, Borum P. Buchman A. Fessler T. A. Howard L. Shenkin A. Valentine C. J., A Call to Action to Bring Safer Parenteral Micronutrient Products to the U.S. Market, Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, 30, 559-69, 2015	Paper is a discussion of the already included ASPEN position paper: "Recommendations for changes in commercially available parenteral multivitamin and multi-trace element products".
Wales, P. W., Allen, N., Worthington, P., George, D., Compher, C., Teitelbaum, D., A.S.P.E.N. Clinical Guidelines: Support of Pediatric Patients	Recommendations were checked and no relevant recommendations matching the areas of interest specified in the protocol were

Excluded studies - 9.1 General principles chapter	
Study	**Reason for exclusion**
with Intestinal Failure at Risk of Parenteral Nutrition-Associated Liver Disease, Journal of Parenteral and Enteral Nutrition, 38, 538-557, 2014	identified. The guideline reports recommendations for paediatric patients with intestinal failure only. Paper does not match eligibility criteria.
Weimann, A., Ebener, C., Holland-Cunz, S., Jauch, K. W., Hausser, L., Kemen, M., Kraehenbuehl, L., Kuse, E. R., Laengle, F., Surgery and transplantation - Guidelines on Parenteral Nutrition, Chapter 18, German medical science : GMS e-journal, 7, 2009	Recommendations were checked and no relevant recommendations matching the areas of interest specified in the protocol were identified. The guideline reports recommendations for parenteral nutrition after surgery and transplantation. Guideline does not match eligibility criteria.
Western Australia Women and Newborn Health Service, Parenteral Nutrition, 2016	**The guideline does not match the eligibility criteria. It was not classified as "high quality" according to pre-specified criteria of 2 domains >70% with appraisal using AGREE II. Scope and purpose: 28%; stakeholder involvement: 17%; rigour of development: 9%; clarity of presentation: 25%; applicability: 23%; editorial independence: 0%.**
Zhu, X. M., Qian, S. Y., Lu, G. P., Xu, F., Wang, Y., Liu, C. F., Ren, X. X., Zhang, Y. C., Gao, H. M., Zhou, T., Dang, H. X., Zhang, C. F., Zhu, Y. M., Chinese guidelines for the assessment and provision of nutrition support therapy in critically ill children, World Journal of Pediatrics, 14, 419-428, 2018	Guideline does not include the population of interest, as specified in the protocol. Guideline includes recommendations for critically ill children aged greater than 1 month only. Therefore it does not match eligibility criteria.

Economic studies

No economic evidence was identified for this review question. See supplementary material D for further information.

Appendix L – Research recommendations

Research recommendations for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

No research recommendations were made for this review question.

Appendix M – Nominal group technique

Additional information related to review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Nominal group technique questionnaire for review question: General principles for neonatal parenteral nutrition

Name:										
Overall level of included vitamins (lipid soluble and water soluble)										
	Strongly disagree								**Strongly agree**	**Insufficient knowledge**
1. Give parenteral vitamins to infants receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										
2. Give parenteral vitamins daily to infants receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										
3. Give parenteral vitamins as multivitamin products to infants receiving parenteral nutrition, where possible.	1	2	3	4	5	6	7	8	9	☐
Comments:										
4. Parenteral vitamins may be given to infants receiving parenteral nutrition as multivitamin products or as individual vitamin products.	1	2	3	4	5	6	7	8	9	☐

Comments:										
5. To improve vitamin stability, administer parenteral vitamin preparations together with the lipid emulsion or a mixture containing lipids.	1	2	3	4	5	6	7	8	9	☐
Comments:										
6. Due to potential vitamin losses when given with a water-soluble solution, parenteral lipid soluble vitamins should be given with the lipid emulsion whenever possible.	1	2	3	4	5	6	7	8	9	☐
Comments:										
7. Due to the hypothetical risk of adverse effects from transient high levels, intermittent substitution of parenteral vitamins is not recommended.	1	2	3	4	5	6	7	8	9	☐
Comments:										
General practice for intravenous fluid volume										
	Strongly disagree								**Strongly agree**	**Insufficient knowledge**
8. Gradually increase fluid intake in infants after birth.	1	2	3	4	5	6	7	8	9	☐
Comments:										
9. Gradually increase fluid intake in preterm and term neonates in the immediate postnatal phase.	1	2	3	4	5	6	7	8	9	☐
Comments:										

Overall levels of blood and urinary electrolytes (Na, K, Cl)										
	Strongly disagree								Strongly agree	Insufficient knowledge
10. Due to the fluid intake replacing only the estimated losses in premature infants <1500g receiving parenteral nutrition, electrolyte supplementation may not be required in the first 5–7 days after birth.	1	2	3	4	5	6	7	8	9	☐
Comments:										
11. Give electrolyte supplementation to infants receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										
12. Begin electrolyte supplementation in infants receiving parenteral nutrition during the transition phase (contraction of extracellular fluid compartment/initial loss of body weight).	1	2	3	4	5	6	7	8	9	☐
Comments:										
13. Maintain electrolyte homoeostasis while the infant is receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										

Overall level of Magnesium										
	Strongly disagree								Strongly agree	Insufficient knowledge

14. Provide Magnesium to infants receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										
15. Preterm infants on early parenteral nutrition during the first days of life may require lower amounts of magnesium, compared to growing stable preterm infants.	1	2	3	4	5	6	7	8	9	☐
Comments:										
16. Adapt magnesium intakes to postnatal blood concentrations in infants receiving parenteral nutrition who have been exposed to maternal magnesium therapy.	1	2	3	4	5	6	7	8	9	☐
Comments:										
17. Provide additional supplementation of magnesium for long term parenteral nutrition in infants when enteral nutrition provides 50% of the energy or less.	1	2	3	4	5	6	7	8	9	☐
Comments:										
Overall level of trace elements (Zinc, Fluoride, Selenium, Copper, Chromium, Iodine, Manganese and Molybdenum)										
	Strongly disagree								**Strongly agree**	**Insufficient knowledge**
18. Give parenteral trace elements to infants receiving parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐
Comments:										
19. Give parenteral trace elements to infants receiving long-term parenteral nutrition.	1	2	3	4	5	6	7	8	9	☐

Comments:										
20. Provide additional trace element supplementation to infants receiving long-term parenteral nutrition when enteral nutrition provides 50% of the energy or less.	1	2	3	4	5	6	7	8	9	☐
Comments:										
21. Commence trace element supplementation in parenteral nutrition for premature infants <1500g when the infant begins gaining weight.	1	2	3	4	5	6	7	8	9	☐
Comments:										
22. Commence trace element supplementation in parenteral nutrition for premature infants <1500g on day 5 of life.	1	2	3	4	5	6	7	8	9	☐
Comments:										
23. Give parenteral trace elements as multi-trace element products for infants receiving parenteral nutrition, where possible.	1	2	3	4	5	6	7	8	9	☐
Comments:										
24. Parenteral trace elements may be given to infants receiving parenteral nutrition as multi-trace element products or as individual trace element products.	1	2	3	4	5	6	7	8	9	☐
Comments:										
Delivery of lipids via syringe or bags										
	Strongly disagree								**Strongly agree**	**Insufficient knowledge**

25. For parenteral solutions administered through a terminal filter, lipid emulsions (or all-in-one mixes) may be passed through a membrane pore size of 1.2-1.5 µm, and aqueous solutions may be passed through a 0.22 µm filter.	1	2	3	4	5	6	7	8	9	☐
Comments:										
Filtration and protection from light										
	Strongly disagree								**Strongly agree**	**Insufficient knowledge**
26. Protect bags and administration sets for use in infant parenteral nutrition from light.	1	2	3	4	5	6	7	8	9	☐
Comments:										
27. To prevent the generation of oxidants, parenteral solutions for premature infants should be protected against light.	1	2	3	4	5	6	7	8	9	☐
Comments:										
28. Protect intravenous lipid emulsions for infant parenteral nutrition by validated light-protected tubing.	1	2	3	4	5	6	7	8	9	☐
Comments:										

Consensus statements with percentage agreement

Table 7: Round 1 statements with percentage agreement for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Statement number	Statement	Consensus percentage in round 1	Action taken
	Overall level of included vitamins		
1.	Give parenteral vitamins to infants receiving parenteral nutrition.	92%	Carried forward to committee discussion
2.	Give parenteral vitamins daily to infants receiving parenteral nutrition.	100%	Carried forward to committee discussion
3.	Give parenteral vitamins as multivitamin products to infants receiving parenteral nutrition, where possible.	73%	Carried forward to round 2
4.	Parenteral vitamins may be given to infants receiving parenteral nutrition as multivitamin products or as individual vitamin products.	50%	Discarded after round 1
5.	To improve vitamin stability, administer parenteral vitamin preparations together with the lipid emulsion or a mixture containing lipids.	80%	Carried forward to round 2
6.	Due to potential vitamin losses when given with a water-soluble solution, parenteral lipid soluble vitamins should be given with the lipid emulsion whenever possible.	55%	Carried forward to round 2
7.	Due to the hypothetical risk of adverse effects from transient high levels, intermittent substitution of parenteral vitamins is not recommended.	17%	Discarded after round 1
	General practice for intravenous fluid volume		
8.	Gradually increase fluid intake in infants after birth.	67%	Carried forward to round 2
9.	Gradually increase fluid intake in preterm and term neonates in the immediate postnatal phase.	67%	Carried forward to round 2
	Overall levels of blood and urinary electrolytes		
10.	Due to the fluid intake replacing only the estimated losses in premature infants <1500g receiving parenteral nutrition, electrolyte supplementation may not be required in the first 5–7 days after birth.	11%	Discarded after round 1
11.	Give electrolyte supplementation to infants receiving parenteral nutrition.	60%	Carried forward to round 2
12.	Begin electrolyte supplementation in infants receiving parenteral nutrition during the transition phase (contraction of extracellular fluid compartment/initial loss of body weight).	56%	Discarded after round 1
13.	Maintain electrolyte homoeostasis while the infant is receiving parenteral nutrition.	90%	Carried forward to

Statement number	Statement	Consensus percentage in round 1	Action taken
			committee discussion
	Overall level of included minerals (magnesium)		
14.	Provide magnesium to infants receiving parenteral nutrition.	100%	Carried forward to committee discussion
15.	Preterm infants on early parenteral nutrition during the first days of life may require lower amounts of magnesium, compared to growing stable preterm infants.	57%	Discarded after round 1
16.	Adapt magnesium intakes to postnatal blood concentrations in infants receiving parenteral nutrition who have been exposed to maternal magnesium therapy.	17%	Discarded after round 1
17.	Provide additional supplementation of magnesium for long term parenteral nutrition in infants when enteral nutrition provides 50% of the energy or less.	17%	Discarded after round 1
	Overall level of included trace elements		
18.	Give parenteral trace elements to infants receiving parenteral nutrition.	100%	Carried forward to committee discussion
19.	Give parenteral trace elements to infants receiving long-term parenteral nutrition.	90%	Carried forward to committee discussion
20.	Provide additional trace element supplementation to infants receiving long-term parenteral nutrition when enteral nutrition provides 50% of the energy or less.	56%	Carried forward to round 2
21.	Commence trace element supplementation in parenteral nutrition for premature infants <1500g when the infant begins gaining weight.	11%	Discarded after round 1
22.	Commence trace element supplementation in parenteral nutrition for premature infants <1500g on day 5 of life.	22%	Discarded after round 1
23.	Give parenteral trace elements as multi-trace element products for infants receiving parenteral nutrition, where possible.	60%	Carried forward to round 2
24.	Parenteral trace elements may be given to infants receiving parenteral nutrition as multi-trace element products or as individual trace element products.	56%	Carried forward to round 2
	Delivery of lipids via syringe or bags		
25.	For parenteral solutions administered through a terminal filter, lipid emulsions (or all-in-one mixes) may be passed through a membrane pore size of 1.2-1.5 µm, and aqueous solutions may be passed through a 0.22 µm filter.	100%	Carried forward to committee discussion
	Filtration and protection from light		
26.	Protect bags and administration sets for use in infant parenteral nutrition from light.	88%	Carried forward to committee discussion

Statement number	Statement	Consensus percentage in round 1	Action taken
27.	To prevent the generation of oxidants, parenteral solutions for premature infants should be protected against light.	89%	Carried forward to committee discussion
28.	Protect intravenous lipid emulsions for infant parenteral nutrition by validated light-protected tubing.	88%	Carried forward to committee discussion

Table 8: Round 2 statements with percentage agreement for review question: What are the general principles of neonatal parenteral nutrition for preterm and term babies?

Statement number*	Redrafted statement	Consensus percentage in round 2	Action taken
	Overall level of included vitamins		
3.	Give parenteral vitamins as multivitamin products to infants receiving parenteral nutrition.	91%	Carried forward to committee discussion
5.	To improve vitamin stability, administer parenteral vitamin preparations together with the lipid emulsion.	91%	Carried forward to committee discussion
6.	Parenteral lipid soluble vitamins should be given with the lipid emulsion whenever possible to remedy potential losses from vitamin oxidation.	90%	Carried forward to committee discussion
	General practice for fluid volume		
8.	Gradually increase fluid intake in infants receiving parenteral nutrition in the context of the individual needs of the infant such as; nutritional intake, fluid retention, dehydration, excessive water losses and special conditions.	64%	Discarded after round 2
9.	Tailor fluid intake in preterm and term neonates receiving parenteral nutrition according to nutritional requirements and clinical assessment, which can include but is not limited to the monitoring of humidity, specific conditions (for example, CDH), and fluid balance.	82%	Carried forward to committee discussion
	Overall levels of blood and urinary electrolytes		
11.	Give electrolyte supplementation (sodium, potassium, chlorine) to infants receiving parenteral nutrition as indicated by monitoring and clinical requirements.	90%	Carried forward to committee discussion
	Overall level of included trace elements		
20.	Provide trace element supplementation to infants receiving long-term parenteral nutrition when enteral nutrition provides 50% of the energy or less.	50%	Discarded after round 2
23.	Give parenteral trace elements as multi-trace element products for infants receiving parenteral nutrition.	80%	Carried forward to committee discussion
24.	Parenteral trace elements may be given to infants receiving parenteral nutrition as individual trace element products when an individual trace element or a specific set of trace elements are required.	90%	Carried forward to committee discussion

** Statement numbers correspond to the numbering used in round 1 (see Table 7 but the text of each statement incorporates redrafting to take account of comments provided by the committee in round 1)*